Celiac Disease AWARENESS CAMPAIGN
OF THE NATIONAL INSTITUTES OF HEALTH
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CELIAC DISEASE News

FROM THE NATIONAL DIGESTIVE DISEASES INFORMATION CLEARINGHOUSE

Celiac Disease Awareness Campaign • www.celiac.nih.gov
A service of the National Institute of Diabetes and Digestive and Kidney Diseases, NIH
Summer 2011

NIH-funded Scientists Discover Gluten-degrading Microbes in the Mouth

Microorganisms that naturally occur in the mouth could potentially render gluten harmless to people with celiac disease, according to research funded in part by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Gluten is the protein in wheat and other common grains that, when consumed by people with celiac disease, elicits an inflammatory immune response in the small intestine.

"This is the first reported evidence for gluten-degrading microorganisms associated with the upper gastrointestinal tract," wrote Eva J. Helmerhorst, Ph.D., associate professor, Henry M. Goldman School of Dental Medicine, Boston University, and co-authors in their report, which appeared October 2010 in the online journal *PloS One*. "Such microorganisms may play a hitherto unappreciated role in the digestion of dietary gluten and thus protection from celiac disease in subjects at risk."

Celiac disease can cause a variety of seemingly unrelated symptoms, including chronic diarrhea, bloating, constipation, weight loss, joint pain, skin rashes, bone loss, and infertility. Of the estimated 1 percent of Americans with celiac disease, many are unaware they have the disease. The principal treatment for celiac disease is a strict, gluten-free diet, which for many is difficult to attain.

Foods that don't normally contain gluten are often contaminated during processing or preparation. Eating even trace amounts of gluten can cause symptoms.

But when sufficiently broken down, gluten no longer stimulates the immune system. Protein-digesting enzymes made by the human body, unfortunately, are not efficient at breaking down gluten. By contrast, enzymes produced by some microorganisms are good at digesting gluten.

GLUTEN-DEGRADING MICROBES,
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NIDDK
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"Apart from interesting biological findings, these bacteria and enzymes may lead to novel and effective strategies to detoxify immunogenic gluten peptides prior to reaching the proximal small intestine."

Eva J. Helmerhorst, Ph.D.
Associate Professor, Henry M. Goldman School of Dental Medicine, Boston University, and co-authors

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The scientists tested the ability of enzymes derived from dental plaque—bacterial deposits that form on teeth—to break down gliadin, the specific gluten protein to which the body's immune system reacts. Dental plaque was removed from volunteers who hadn't brushed their teeth for 48 hours and suspended in a salivalike solution. The scientists added various natural and synthetic gliadins to the samples and measured their degradation over time.

Results showed that samples containing dental plaque exhibited high gliadin-degrading enzymatic activity, compared with saliva samples without dental plaque. Importantly, dental plaque degraded two gliadin protein segments known to stimulate the immune system and cause celiac disease symptoms. One of these protein segments, known as superantigen, was also degraded by human-produced enzymes; however, proteolytic efficiency varied significantly among volunteers, implying some people are better at breaking down gliadin than others.

"Apart from interesting biological findings, these bacteria and enzymes may lead to novel and effective strategies to detoxify immunogenic gluten peptides prior to reaching the proximal small intestine," wrote Helmerhorst and co-authors.

One strategy proposed by the authors is to develop gluten-degrading probiotics. Probiotics, sometimes called friendly bacteria, are

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Would you like to know more about NIDDK-supported research?

The National Institutes of Health (NIH) provides access to a variety of reporting tools, reports, data, and analyses of NIH research activities at the Research Portfolio Online Reporting Tools (RePORT) website, *www.projectreporter.nih.gov/reporter.cfm*. One of the tools available is RePORT Expenditures and Results (RePORTER), which allows users to search a repository of NIH-funded research projects and access and download publications and patents resulting from NIH funding. ■

CELIAC DISEASE News

Celiac Disease News, an email newsletter, is sent to subscribers by the National Digestive Diseases Information Clearinghouse (NDDIC). The newsletter features news about celiac disease, special events, patient and professional meetings, and new publications available from the NDDIC and other organizations.

Please visit *www.celiac.nih.gov/Newsletter.aspx* to read or download a PDF version or to subscribe to the newsletter.

The National Institutes of Health Celiac Disease Awareness Campaign provides current, comprehensive, science-based information about the symptoms, diagnosis, and treatment of celiac disease, also known as celiac sprue, nontropical sprue, and gluten-sensitive enteropathy. The Awareness Campaign is an initiative of the NDDIC, a service of the National Institute of Diabetes and Digestive and Kidney Diseases.

Visit *www.celiac.nih.gov* to learn more about the Awareness Campaign.

Executive Editor: Stephen P. James, M.D.

Dr. James is the director of the Division of Digestive Diseases and Nutrition within the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). As director, Dr. James oversees planning, implementation, and evaluation of a national research effort focused on gastrointestinal, pancreatic, hepatobiliary, and nutrition diseases and conditions. Before joining the NIDDK in 2001, Dr. James directed the division of gastroenterology at the University of Maryland's School of Medicine for 10 years.

Antibodies to Non-gluten Wheat Components May Predict Celiac Disease

Production of antibodies to Glo-3A, a non-gluten component of wheat, may predict celiac disease, according to scientists funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). In a study of children at high risk of developing the autoimmune disease, which attacks cells lining the small intestine, high levels of antibodies to Glo-3A were detectable in blood earlier than antibodies to tissue transglutaminase (TTG), a serologic marker frequently used to diagnose celiac disease. The finding offers the potential for better celiac disease screening.

"These results may indicate that the immune pathology and subsequent damage that are characteristic of celiac disease start early in life."

Craig E. Taplin
Research Fellow, Barbara Davis Center for Childhood Diabetes, University of Colorado, and co-authors

"The present study shows that higher levels of Glo-3A antibodies are associated with celiac disease both at the time of clinical diagnosis and before that point," wrote Craig E. Taplin, a research fellow at the Barbara Davis Center for Childhood Diabetes at the University of Colorado, and co-authors.

The study, which appeared in the February 2011 issue of *The Journal of Pediatric Gastroenterology and Nutrition,* came from the Celiac Disease Autoimmunity Research (CEDAR) Study aimed at finding the genetic and environmental causes of celiac disease and better diagnostic strategies.

When diagnosing celiac disease, health care providers typically screen patients' blood for the presence of TTG antibodies. TTG is an enzyme that alters the gliadin molecule by deamidating glutamine residues; these residues in turn bind to antigen presenting cells and activate T cells, leading to damage to the fingerlike cells called villi that line the small intestine. Over time, the cellular damage, known as villous atrophy, leads to malabsorption of food, gastrointestinal bloating, and diarrhea. But by the time TTG antibodies are detectable, villous atrophy has often already begun—prompting scientists to look for diagnostic tools that allow earlier diagnosis.

Glo-3A, is a storage protein found in wheat. The scientists compared Glo-3A antibody blood levels in two groups of children, matched by age, race, ethnicity, and celiac disease risk factors. One group tested positive for TTG antibodies—i.e., had celiac disease—whereas the matched control group did not have celiac disease.

Blood was collected before each child's first birthday and then at least once each year thereafter. Results showed that the children with celiac disease had higher levels of Glo-3A antibodies, and this difference was apparent well before TTG autoantibodies appeared. Glo-3A antibody production in the celiac group appeared, on average, about 2 years before TTG antibodies were detectable, at around age 3 versus age 5 for TTG antibodies.

The function of Glo-3A antibodies and whether they play a role in celiac disease are unclear. In their report, the researchers interpreted Glo-3A antibody expression two possible ways:
1. The Glo-3A antibody response is a reflection of increased diversity in the child's diet; or
2. Glo-3A antibody production is a biomarker of impaired immune tolerance and increased gut permeability, i.e., celiac disease.

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Gluten-degrading Microbes, continued from page 2

microorganisms added to foods for anticipated health benefits. Such an approach, according to the scientists, could render foods contaminated with minor amounts of gluten safe for people with celiac disease.

Scientists are already conducting clinical trials to test this approach using bacteria isolated from plants. Human-derived microorganisms, according to the scientists, might offer greater potential as a probiotics source because they are adapted to a human host environment. Plaque-derived enzymes were found to be active over a broad pH range, suggesting they could continue breaking down gliadin not only in the mouth but throughout the gastrointestinal tract, including the acidic stomach and small intestine.

Helmerhorst and colleagues are working to identify and characterize the specific strains of bacteria that contribute to plaque's gluten-degrading ability. They have already found four strains whose activity far exceeds the mixture of plaque bacteria described in their report.

Major funding was provided by the National Institute of Allergy and Infectious Diseases, part of the NIH.

For more information about clinical trials involving the use of plant-derived probiotics in people with celiac disease, search for NCT00810654 or NCT00959114 at *www.ClinicalTrials.gov.*

The NIH Celiac Disease Awareness Campaign provides current, comprehensive, science-based information about the symptoms, diagnosis, and treatment of celiac disease, also known as celiac sprue, nontropical sprue, and gluten-sensitive enteropathy. For more information, visit *www.celiac.nih.gov.* ■

Non-gluten Wheat, continued from page 3

"These results may indicate that the immune pathology and subsequent damage that are characteristic of celiac disease start early in life," wrote Taplin and co-authors. To identify possible diagnostic utility, however, "it is necessary to measure Glo-3A antibodies in a larger sample of children from the general population to establish normal and abnormal levels."

The CEDAR Study is an ancillary project of Diabetes Autoimmunity Study in the Young (DAISY), which is also funded by the NIDDK. Type 1 diabetes and celiac disease have similar genetic origins: Up to 16 percent of children with type 1 diabetes also have celiac disease. DAISY has followed more than 2,000 children at high risk of developing type 1 diabetes and celiac disease, based on genetic testing or having a first-degree relative with type 1 diabetes. Children in DAISY are followed from birth until diabetes onset or age 15.

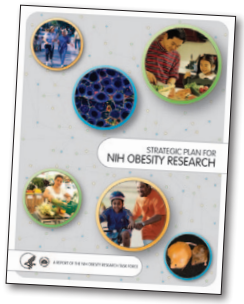
More information about the Genetic and Environmental Causes of Celiac Disease project can be found by searching for project number 5R01DK050979–14 on the National Institutes of Health (NIH) RePORTER website at *www.projectreporter.nih.gov/reporter.cfm.*

The NIH RePORTER website allows users to search a repository of NIH-funded research projects and access and download publications and patents resulting from NIH funding.

For more information about DAISY, visit *www.daisycolorado.org.*

The National Digestive Diseases Information Clearinghouse disseminates information about celiac disease through the NIH Celiac Disease Awareness Campaign. For more information, visit the campaign website at *www.celiac.nih.gov.* ■

Strategic Plan for NIH Obesity Research Seeks to Curb Epidemic



In March 2011, the National Institutes of Health (NIH) released the comprehensive *Strategic Plan for NIH Obesity Research.* The plan was assembled by health care professionals, researchers, and the public to combat the obesity epidemic. More than one-third of U.S. adults and nearly 17 percent of U.S. children are obese. Obesity increases health risks such as type 2 diabetes, heart disease, high blood pressure, fatty liver disease, and cancer.

"Obesity has many causes and contributing factors. This plan is a bold blueprint that will encourage the research community to examine the epidemic of obesity from diverse perspectives," said NIH Director Francis S. Collins, M.D., Ph.D. "Through the scientific opportunities outlined in the strategic plan, researchers can work together toward the goals of preventing and treating obesity, to help people lead healthier and more fulfilling lives."

The plan recognizes that eating less and exercising more is easier said than done. Highlighting the crucial role of research in efforts to reduce obesity, the plan emphasizes using education and outreach to move proven research strategies from the laboratory into clinical trials and ultimately into practical solutions for community programs and medical practice. Recommendations include

- discovering the key processes that regulate body weight and influence behavior
- understanding the factors that contribute to obesity and its consequences
- designing and testing new approaches for achieving and maintaining a healthy weight
- evaluating promising strategies to prevent and treat obesity in real-world settings and diverse populations
- using technology to advance obesity research and improve health care delivery

The *Strategic Plan for NIH Obesity Research* was developed by the NIH Obesity Research Task Force, which is co-chaired by Griffin P. Rodgers, M.D., M.A.C.P., director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); Susan B. Shurin, M.D., acting director of the National Heart, Lung, and Blood Institute; and Alan E. Guttmacher, M.D., director of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development.

Though there is no funding directly tied to the plan, NIH funds research to better understand the causes and consequences of obesity and to develop and test new prevention and treatment strategies, an investment of $824 million in fiscal year 2010, plus awards totaling $147 million made in the same year through the American Recovery and Reinvestment Act of 2009.

To order or download the *Strategic Plan for NIH Obesity Research* or the 8-page nontechnical summary, visit *www.obesityresearch.nih.gov.*

The NIH offers free tools, tips, and resources to help people achieve or maintain a healthy weight through the NIDDK Weight-control Information Network. For more information visit *www.win.niddk.nih.gov.* ■

NIH Launches Bowel Control Awareness Campaign for Health Care Professionals and the Public

On June 1, 2011, the National Institutes of Health (NIH) launched the Bowel Control Awareness Campaign to raise awareness of bowel control problems, also known as fecal incontinence. A bowel control problem is a mild to severe inability to control bowel movements. The Awareness Campaign stems from the recommendations of an independent panel of experts convened by the NIH to assess the current prevalence, risk factors, diagnosis, treatment, and management of the condition.

NIDDK Bowel Control Awareness Campaign materials

"People experiencing bowel control problems need to know they are not alone and that the condition can be managed. The Bowel Control Awareness Campaign will inform health care professionals and the public that bowel incontinence is a common condition and that effective treatments are available."

Stephen P. James, M.D.
Director, Division of Digestive Diseases and Nutrition, NIDDK

"Our findings indicate that fecal incontinence is a significant public health burden in the U.S.—affecting close to 10 percent of the adult population over 40 years old," said Griffin P. Rodgers, M.D., M.A.C.P., director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the NIH Institute leading the effort. "The Bowel Control Awareness Campaign's main objective is raising public awareness of fecal incontinence to aid in prevention of incontinence and to improve the lives of men and women living with the condition."

Bowel control problems affect an estimated 18 million U.S. adults—one out of 12 people. People with bowel control problems are often reluctant to discuss the condition with their doctor. The embarrassment associated with fecal incontinence can have a crippling effect on quality of life for millions, and the condition is believed to be widely underdiagnosed.

Developed by the NIDDK, along with professional and voluntary organizations, the Awareness Campaign offers materials and resources about the symptoms, diagnosis, treatment, and management of bowel control problems for patients and health care professionals. Available through the Awareness Campaign's "Let's Talk about Bowel Control" website are publications such as a fecal incontinence fact sheet, an easy-to-read bowel control booklet, and a health fair flyer; NIH bowel control research information; and links to professional and voluntary organizations.

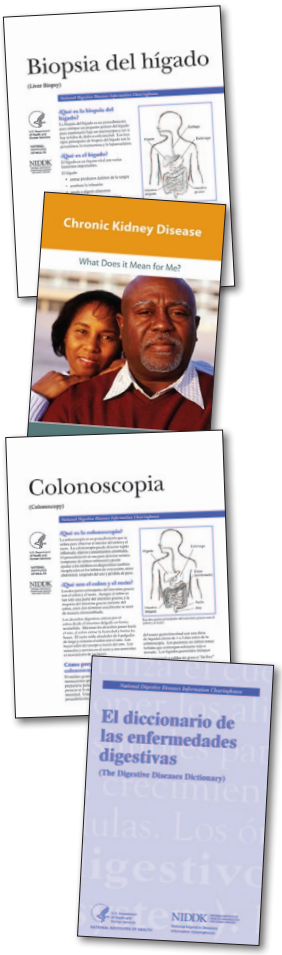
"The lack of communication between health care professionals and patients appears to be one of the main challenges with bowel control problems. Being able to talk about the problem is the first step in both prevention and treatment," said Stephen P. James, M.D., director of the Division of Digestive Diseases and Nutrition at the NIDDK. "People experiencing bowel control problems need to know they are not alone and that the condition can be managed. The Bowel Control Awareness Campaign will inform health care professionals and the public that bowel incontinence is a common condition and that effective treatments are available."

For more information about the Bowel Control Awareness Campaign, or to download any of the campaign materials, visit the website at *www.bowelcontrol.nih.gov.*

For health information about digestive diseases, visit the National Digestive Diseases Information Clearinghouse, part of the NIDDK, at *www.digestive.niddk.nih.gov.* ■

NIDDK Health Information Resources Win NIH Plain Language/Clear Communication Awards

Six health information resources produced by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) won 2010–2011 National Institutes of Health (NIH) Plain Language and Clear Communication awards. The annual awards program, now in its 11th year, honors communication products that help the NIH reach all Americans with health information they can use and research results they can easily understand.



2010–2011 NIDDK NIH Plain Language/Clear Communication Award winners:

Biopsia del hígado (Liver Biopsy), produced by the National Digestive Diseases Information Clearinghouse (NDDIC), is a Spanish-language fact sheet that provides general information about liver biopsy: the purpose of the test, how to prepare for it, and what to expect during and after the procedure. The fact sheet is also available in English. To view, download, or order the fact sheet, visit the NDDIC website at *www.digestive.niddk.nih.gov.*

Chronic Kidney Disease: What Does it Mean for Me?, produced by the National Kidney Education Program (NKDEP), is a full-color brochure designed to help recently diagnosed patients understand chronic kidney disease. View, download, or order the brochure at the NKDEP's website, *www.nkdep.nih.gov/resources/CKD_Basics_brochure.htm.*

Colonoscopia (Colonoscopy), produced by the NDDIC, is a Spanish-language fact sheet that provides general information about colonoscopy: the purpose of the test, how to prepare for it, and what to expect during and after the procedure. The fact sheet is also available in English. To view, download, or order the fact sheet, visit the NDDIC website at *www.digestive.niddk.nih.gov.*

El diccionario de las enfermedades digestivas (The Digestive Diseases Dictionary), produced by the NDDIC, is a Spanish-language booklet that defines more than 400 terms and includes illustrations. The booklet is also available in English. To view, download, or order the booklet, visit the NDDIC website at *www.digestive.niddk.nih.gov.*

Healthy Moments is a weekly radio report series from NIDDK Director Griffin P. Rodgers, M.D., M.A.C.P. The series, broadcast online and on radio, provides health tips about how to prevent and control diseases that fall within the NIDDK's purview. For more information and to listen to new and archived reports, visit *www2.niddk.nih.gov/HealthEducation/HealthyMoments.*

The National Diabetes Education Program's (NDEP's) Managing Your Diabetes campaign materials, based on health messaging research and focus groups, reinforce the seriousness of diabetes and the importance of managing diabetes as early as possible. The materials, including posters and public service announcements, were developed for NDEP partners and media outlets and feature people living with diabetes. Visit the NDEP website for more information about the campaign and to access campaign materials at *www.ndep.nih.gov.*

The NDEP's Managing Your Diabetes podcasts series features real people living with diabetes and shares their personal stories about how they manage their diabetes every day. Visit the NDEP website for more information and to access the podcasts at *www.ndep.nih.gov.*

Information about the NIH Plain Language/Clear Communication Awards program and a complete list of winners is available at *www.nih.gov/clearcommunication/plainlanguage.htm.* ■

2011 Edition of NIDDK's Annual Scientific Report Now Available

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) annual scientific report, *NIDDK Recent Advances & Emerging Opportunities,* is now available. This report highlights examples of NIDDK-supported research advances published in fiscal year 2010. The report includes "Stories of Discovery," which traces research progress in specific areas over a longer time frame, and profiles of patients who are benefiting from NIDDK-supported clinical research. This year's report also contains a special section highlighting the NIDDK's 60th anniversary activities, as well as a feature about the 2010 Albert Lasker Basic Medical Research Award winners—current and former NIDDK grantees Jeffrey Friedman, M.D., Ph.D., and Douglas Coleman, Ph.D.

To read the report online, visit *www2.niddk.nih.gov/AboutNIDDK/ResearchAndPlanning/Advances/FY2011.* To request a copy, fill out the form at *www.catalog.niddk.nih.gov/ContactUs.cfm,* call 1–800–860–8747, or write to the NIDDK Clearinghouses Publications Catalog, 5 Information Way, Bethesda, MD 20892–3568.

The NIDDK has health information, including easy-to-read booklets and fact sheets. For more information or to obtain copies, visit *www.niddk.nih.gov.* ■

NIDDK Staff Update

Padma Maruvada, Ph.D., joined the Division of Digestive Diseases and Nutrition as the new director of the Nutrition and Clinical Obesity Program. Maruvada served as the program officer in the National Center for Research Resources for the Institutional Development Awards Program, where she managed a multidisciplinary research portfolio. She also served as program director in the National Cancer Institute's Division of Cancer Prevention. Maruvada trained in the National Institute of Diabetes and Digestive and Kidney Diseases' intramural research program. ■

In Memoriam

Vanessa Z. Ameen, M.D., a senior scientific advisor within the Division of Digestive Diseases and Nutrition, died in February 2011. Specializing in pediatrics and gastroenterology, Ameen was recruited to the National Institutes of Health (NIH) from private industry, where she served as medical director to several pharmaceutical manufacturers. Ameen was previously an assistant professor of pediatrics at Temple University, and she taught at Indiana University and the Medical College of Wisconsin. Ameen served as science officer for the Patient-Reported Outcomes Measurement Information System (PROMIS), a network of NIH-funded facilities working to develop better measures for patient symptom-based outcomes. ■

New Publications

Celiac Disease

"Dental Enamel Defects and Celiac Disease," was re-released in May 2011 in support of Celiac Disease Awareness Month. The 2-page feature article explains that celiac disease, although often considered a digestive disorder, causes a variety of problems outside the gastrointestinal tract, including dental enamel defects such as discolored spots, pitting or banding of teeth, and mottled or translucent-looking teeth.

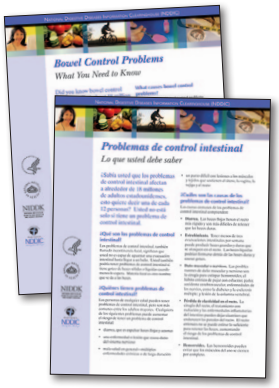
The article originally appeared in the National Institutes of Health Celiac Disease Awareness Campaign's newsletter, *Celiac Disease News,* and was updated for print and distribution at health fairs and health care providers' offices.

To view, download, or order copies, or to learn more about the Awareness Campaign, visit *www.celiac.nih.gov.*

Bowel Control

In support of the Bowel Control Awareness Campaign, a service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Digestive Diseases Information Clearinghouse (NDDIC) has released two new publications about bowel control problems.

What I need to know about Bowel Control is a 28-page, easy-to-read booklet that defines bowel control problems and explains how normal bowel control works. The booklet provides helpful tips for talking with health care providers and coping with bowel control problems. The booklet is available in English and Spanish.



Bowel Control Problems: What You Need to Know, part of the NIDDK Awareness and Prevention Series, provides a brief overview of the causes, diagnosis, and treatment of bowel control problems. The 4-page, printed fact sheet includes English and Spanish versions and is perfect for distribution at health fairs and health care providers' offices.

To view, download, or order copies, or to learn more about the Awareness Campaign, visit *www.bowelcontrol.nih.gov.*

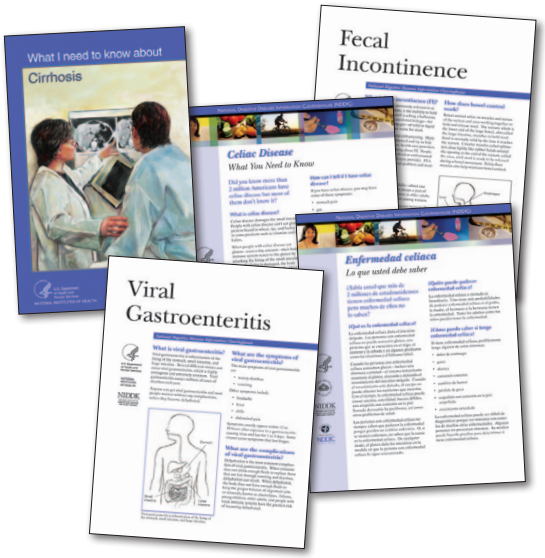
These publications are also available at *www.digestive.niddk.nih.gov.*

Updated Publications

The NDDIC has updated the following publications:

- *Celiac Disease: What You Need to Know* (English and Spanish)
- *Diarrhea*
- *Fecal Incontinence*
- *Hemorrhoids*
- *Viral Gastroenteritis*
- *What I need to know about Celiac Disease* (English and Spanish)
- *What I need to know about Cirrhosis* (English and Spanish)
- *What I need to know about Diarrhea*

These publications are available at *www.digestive.niddk.nih.gov.*



Upcoming Meetings, Workshops, and Conferences

The National Institute of Diabetes and Digestive and Kidney Diseases Information Clearinghouses will exhibit at the following upcoming event:

American College of Gastroenterology Scientific Meeting

October 28–November 2 in Washington, D.C.
For more information, visit *www.acg.gi.org*. ■

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